PATENT COOPERATION TREATY

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference NRS/LP6090359	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/GB 03/05223	International filing date *(day/month/year)* 28.11.2003	Priority date *(day/month/year)* 29.11.2002
International Patent Classification (IPC) or both national classification and IPC C12Q1/68		
Applicant UCL BIOMEDICA PLC et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 12 sheets.

3. This report contains indications relating to the following items:

I	☒	Basis of the opinion
II	☐	Priority
III	☒	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
IV	☐	Lack of unity of invention
V	☒	Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
VI	☐	Certain documents cited
VII	☐	Certain defects in the international application
VIII	☐	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
13.07.2004	04.04.2005
Name and mailing address of the international preliminary examining authority: European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016	Authorized Officer Gabriels, J Telephone No. +31 70 340-4282

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB 03/05223

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-59 as originally filed

Claims, Numbers

1-64 received on 13.07.2004 with letter of 09.07.2004

Drawings, Sheets

1/10-10/10 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).

   ☐ the language of publication of the international application (under Rule 48.3(b)).

   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☐ contained in the international application in written form.

   ☐ filed together with the international application in computer readable form.

   ☒ furnished subsequently to this Authority in written form.

   ☒ furnished subsequently to this Authority in computer readable form.

   ☒ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☒ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:

   ☒ the claims, Nos.: 65-75

   ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

   ☐ the entire international application,

   ☒ claims Nos. 36-48, 54, 57-64

   because:

   ☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (specify):

   ☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

   ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

   ☒ no international search report has been established for the said claims Nos. 36-48, 54, 57-64

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

   ☐ the written form has not been furnished or does not comply with the Standard.

   ☐ the computer readable form has not been furnished or does not comply with the Standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-35,49-53,55,56
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-35,49-53,55,56
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-35,49-53,55,56
	No:	Claims	

2. Citations and explanations

   see separate sheet

I. Basis (Continuation)

Sequence listing pages 1-28 filed with the letter of 04/03/2004 do not form part of the application (Rule 13ter.1(f) PCT).

III. Non-establishment of opinion (Continuation)

Claims 36-48, 54, 57-64 have not been searched. The applicant is reminded that claims or parts thereof for which no International Search Report has been established, will not be the subject of the International Preliminary Examination (Rules 66 (1) (e); 70 (2) (d) PCT).

V. Reasoned statement (Continuation)

2.1 CITATIONS

Reference is made to the following documents:

D1: WO-A-0231209
D2: WO-A-0154477
D3: Journal Of Human Genetics (2002), 47(11), 605-610
D4: Nature Genetics, Nature America, New York, Us (03-1999), 21, 323-325

2.2 REMARKS

2.2.1 The independent method claims 1 and 10 do not enable the skilled person to perform the methods claimed because the cancer associated plexinB1 mutations are not clearly defined. These claims refer to mutations that are located in the coding region of plexinB1. However, the plexinB1 protein consists of 2135 AA and the 17 mutations described in the present application are all located between AA 1597 and AA 1904. The clustering of these mutations in this region does not indicate that any mutation of the plexinB1 coding region is associated with cancer. Examination of these claims with respect to novelty and inventive step is therefore performed based on the mutations defined in claims 4-6.

2.2.2 The same reasoning (c.f. 2.2.1) can be made for the independent claims 19, 49, 50, 55, and 56.

2.2.3 For these reasons claims 1, 10, 19, 49, 50, 55, and 56 lack clarity according to Art. 6 PCT taken in combination with Rule 6.3 (b) PCT (see also PCT Preliminary Examination Guidelines III.4.3).

2.3 NOVELTY (Art. 33(2) PCT)

2.3.1 D1 discloses methods for identifying and/or obtaining compounds as a putative anti-cancer agents (e.g. prostate cancer). The method comprises contacting a nucleic acid with a test compound and determining the expression of the nucleic acid in the presence relative to the absence of the test compound (cf. claims 52-58). D1 further discloses that the nucleic acid sequence with IMAGE ID:755952 (=plexinB1) is one of the nucleic acid sequences that show temporal expression changes during prostate cancer hormonal therapy and regression. However, after filtering the data this sequence was excluded.

2.3.2 D2 discloses the use of a list of 1009 nucleic acid sequences (among which plexinB1 (cf. table 2 (SEQ ID NO:257 = plexinB1)) for the manufacture of a medicament for the treatment of an extensive list of different disorders (among which cancer). There is however no specific disclosure of a medicament using plexinB1 for the treatment of cancer.

2.3.3 The present application does satisfy the criterion set forth in Article 33(2) PCT because the subject-matter of claims 1-35, 49-53, 55, and 56 is new in respect of prior art as defined in the regulations (Rule 64(1)-(3) PCT).

2.4 INVENTIVE STEP (Art. 33(3) PCT)

2.4.1 Document D1 is considered to represent the most relevant state of the art (cf. 2.3.1). The subject-matter of claim 1 differs in that specific mutations are identified (See remarks 2.2.1-2.2.3) which alter the expression of the plexinB1 gene in cancer.

2.4.2 The problem to be solved by the subject matter of claim 1 may therefore be regarded as providing a method for assessing an individual for a cancer

condition. The solutions would be the specific mutations identified (See remarks 2.2.1-2.2.4).

2.4.3 The skilled person would be aware of the teaching of D1 showing temporal expression changes during prostate cancer hormonal therapy and regression and would probably concentrate on the genes that were not filtered out. Some of the polymorphisms present in this gene are described in D3 and D4. There is however no link between these polymorphisms and cancer. The skilled person would therefore not be encouraged to look at the plexinB1 gene in order to solve the problem posed.

2.4.4 A similar reasoning can be made for independent claims 10, 19, 29, 49, and 55.

2.4.5 In view of the remarks given above (see points 2.2.1-2.2.4), present claims 1-35, 49-53, 55, and 56 satisfy the criterion set forth in Article 33(3) PCT because they involve an inventive step (Rule 65(1)(2) PCT).